TABLE I.
Nitrogen Clearance Data from 5 Control Subjects and 3 Patients with Marked Emphysema.

Subject	Condition	Height, cm	Body wt, kg	N_2 clearance vol., l
D.	Normal	283	63.5	32.8
				32.8
				32.
				32.
J.M.	"	268	66.0	29.2
				27.6
				27.6
J.S.	"	260	59.2	26.8
				26.
				22.8
M.	"	280	75.0	22.8
				22.8
				20.4
				20.4
B.	"	280	77.4	17.6
				17.3
				16.8
				16.
L.	Emphysema	280	63.5	116.
K.	"	264	61.0	120.
A.	"	264	77.5	160.

for those tested. Three cases of marked pulmonary emphysema are presented. The results from testing this group in a similar fashion indicate a prolongation of nitrogen elimination in these patients as compared with the normal subjects.

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Cross Transfusion. II. Therapeutic Effect in Acute Mercury Nephrosis.* (17795)

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Recently, a safe and controllable method for cross transfusion and the instrument for this purpose have been described(1). The difficulties and dangers of earlier methods (2-7), which often caused the death of experimental animals, were encountered when the experiments were repeated by us. Briefly, the difficulties have been:

1. Sacrifice of an artery to obtain blood (2-7). This can be repeated only a few times in the same individual. It is also unsuitable because of the occurrence of arterial spasm, which often terminates the procedure, and because withdrawal of blood from an artery against a low resistance puts an additional load on the heart. Methods which alternately withdraw and administer blood often cause shock(3).

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TABLE I.
Determination of the MLD_{100} of Intravenous $HgCl_2$ in Adult Dogs.

Wt, kg	Sex	Dose $HgCl_2$ mg/kg	Last measured plasma creatinine level mg/100 cc	Survival, days
12.3	M	5.	8.90	1.96
17.5	F	4.	14.90	2.87
16.8	F	3.5	12.89	3.54
18.2	F	3.5	9.20	1.83
20.5	M	3.	7.78	3.50
15.4	M	2.5	8.84	5.00
22.3	M	2.5	20.03	8.75
15.9	M	2.5	6.98	2.62
18.2	M	2.5	21.40	8.13
18.2	M	2.5	10.64	3.41
21.4	M	2.	22.40	8.62
18.1	M	2.	16.06	6.00
10.5	M	2.	15.48	9.76
10.9	F	2.	15.48	8.08
10.5	F	2.	17.20	3.66
15.0	M	2.	1.03	4.50
21.0	F	1.5	1.79	S
5.0	M	2.	.60	S
9.5	F	2.5	.62	S

S—Survived.

2. Roller pumps and worm pumps (6) often cause hemolysis in a ratio of about .1% per single passage of blood through the apparatus. This is a toxic amount in many cases.

3. Clotting and deposition of proteins occur in spite of the use of anticoagulants(6). This slows down and often stops the flow of blood. It also interferes with the metering function of roller pumps because it narrows the blood conduits.

4. The absence of accurate measuring devices for blood flow. A small error becomes magnified over a period of time, leading to oligemia in one organism and plethora in the other, often with fatal results(2-7).

Our apparatus does not injure the blood and withdraws and administers blood continuously and simultaneously through double lumen intravenous catheters. It pumps and measures with a high degree of accuracy the blood flowing in both directions, and automatic electric devices adjust the flow. In order to evaluate the effectiveness of cross transfusion it was decided to study a pathological condition which was easily reproduced, well-known, and capable of quantitative analysis. The intravenous administration of a 100% lethal dose of mercuric chloride was chosen as the test condition.

Methods and procedure: Adult mongrel dogs, varying in weight between 10½ and 23 kg, were used. The mercuric chloride was administered as a 5.00 mg/cc solution in physiological saline given rapidly into the external saphenous vein. Arterial heparinized blood samples were taken at the time of injection and at daily or 48 hour intervals thereafter. Hematocrit determinations of the centrifuged specimens were made and the plasma creatinine was determined by the method of Bonsnes and Tausky(8). Autopsies were performed and the organs preserved in 10% formalin for histological study. Several animals died from causes not attributable to mercury nephrosis or to cross transfusion and are not included here. The following procedure was used: the jugular or femoral vein of each animal was isolated, under local anesthesia, and a double lumen catheter passed cardiad for a distance of about 15 cm. About 3.75 mg of heparin per kg of body weight was injected through the catheter and blood samples were withdrawn. The catheters were then attached to the apparatus which previously been filled with 230 cc of heparinized saline and the cross transfusion started at a rate of 5 to 6 liters an hour in each direction. At the end of the cross

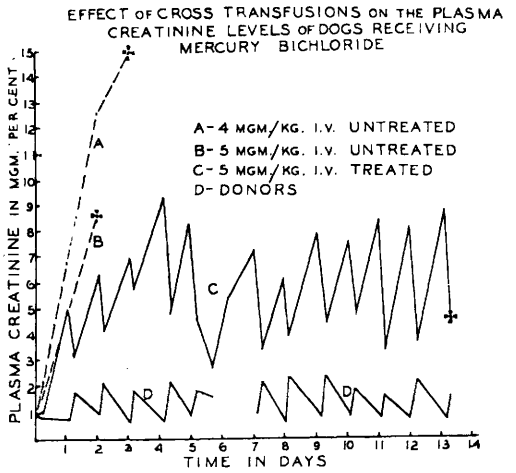
8. Bonsnes, R. W., and Tausky, H. H., *J. Biol. Chem.*, 1945, v158, 581.

transfusion, samples of blood were again taken and the blood in the apparatus was washed into the animals by 100-200 cc isotonic solutions. Additional heparin was added occasionally during the procedure. Animals received sedation in some of the experiments, which had no effect on the results. Cross matching, when done, had no appreciable effect on the outcome of the experiment. Sterile technic is desirable. 150,000 U of procaine penicillin in oil was given as a precautionary measure. The duration of the cross transfusions and the quantity of blood transferred could be varied at will.

Results and discussion. 1. *Determination of the minimum 100% lethal dose of intravenous $HgCl_2$ in the dog* was made by means of 19 animals (Table I).

All the animals weighing more than 10.5 kg that received 2.0 mg $HgCl_2$ or more per kg of body weight died within 10 days. 2.5 mg kg was chosen as the minimum LD100 for full grown dogs weighing 10.5 kg or more, when mercuric chloride is injected rapidly by the intravenous route. This value is not applicable to very young dogs or dogs weighing less than 10.5 kg, as is illustrated in the last two entries in Table I. The textbooks give the figure of 4 mg/kg as the intravenous MLD100 of $HgCl_2$ for the dog. The experiments on which this figure is based were performed by Sansum(9) who gave intravenous injections to 3 dogs "by means of a special pump, so that each injection took exactly thirty minutes to accomplish". This method of injection is different from the customary intravenous injection, which is performed within a few seconds, and it is not surprising, therefore, that Sansum's MLD100 is different from ours.

2. *Evidence of Therapeutic Efficacy of Cross Transfusion.* (a) *Transfusion begun 1-2 days after poisoning with mercuric chloride.* In 5 experiments, animals poisoned from 1-2 days before the first transfusion, were treated repeatedly at intervals of 24 to 120 hours by cross transfusions, lasting 2 to 5 hours, with



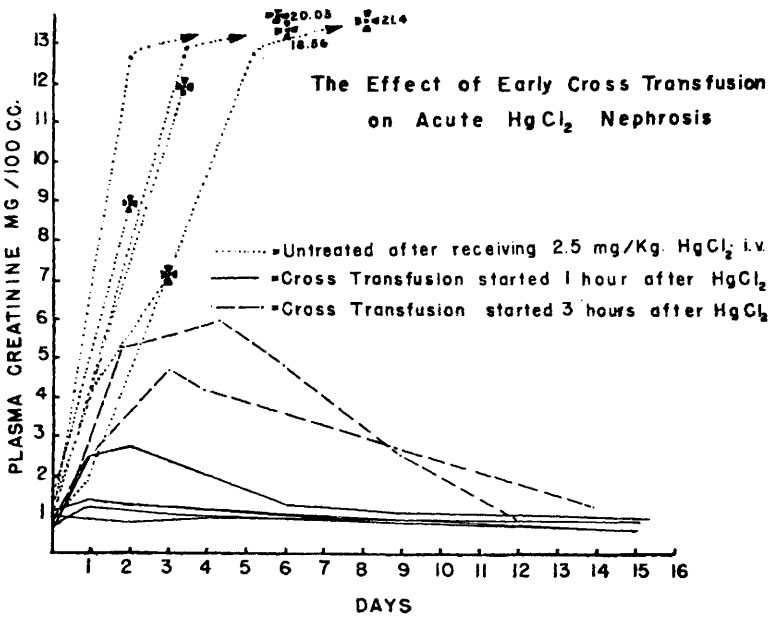
GRAPH 1.

presumably normal donors. In every case the animal was maintained alive for a time 2 to 3 times longer than controls receiving the same dose of $HgCl_2$. One animal which had received 2.5 mg $HgCl_2$ per kg, recovered after 2 cross transfusions. Graph I represents the creatinine levels in one of these experiments and is also illustrative of the others. This animal received 5.0 mg/kg of $HgCl_2$ which was twice the MLD. Each abrupt drop in the plasma creatinine level of the patient is the result of a cross transfusion. At postmortem examination the epithelium of the tubules of both kidneys was completely necrotic and in great part, calcified, without any evidence of regeneration.

The donors showed no signs of injurious effects. Their plasma creatinine levels returned to normal well within 24 hours. The occasional chills, retching, vomiting, and, in two cases, hives, disappeared soon and did not constitute cause for discontinuance of the experiment. Catherized urine specimens did not contain abnormal amounts of protein. It can be observed that the creatinine level of the patient's blood usually dropped more than it rose in the donor's blood. This difference is taken to illustrate the lowering of the plasma creatinine level because of excretion by the donor's kidneys.

(b) *Transfusion begun 1-3 hours after poisoning.* Six animals were given 2.5 mg $HgCl_2$ per kg and then transfused either one

9. Sansum, W. D., *J. A. M. A.*, 1918, v70, 824.



GRAPH II.

hour or 3 hours after the administration of the mercury. Graph II shows the plasma creatinine levels of the animals so treated. The 4 dogs treated at the end of 60-90 minutes remained clinically well and did not show any significant or prolonged elevation of plasma creatinine. Pathological changes were not found on microscopic examination of the kidneys 3 to 6 weeks later. The 2 dogs cross transfused 3 hours after the administration of the $HgCl_2$ showed clinical evidence of mercury poisoning, such as anorexia, vomiting, diarrhea, lassitude and also transitory elevation of blood creatinine, but recovered within 10 days.

The mechanism of action of cross transfusion in preventing a fatal outcome in these animals is not known. We believe that cross transfusion serves to reduce the amount of mercury in the poisoned animal to a sublethal quantity by partial transfer to the donor. As indicated by the discrepancy between Sansum's and our figure for the MLD 100, the donor would not be harmed, because the mercury is received by the donor gradually over a period of time and already partly detoxified. The transfer of detoxifying substances to the poisoned animal from the donor may also play an important part.

Summary. 1. When performed with inadequate equipment, cross transfusion may be a dangerous procedure. However, it has been shown in experiments on dogs, that with proper apparatus and technic, cross transfusion is safe for both donor and patient.

2. For dogs weighing 10.5 kg or more, the intravenous MLD100 of mercuric chloride is 2.5 mg/kg.

3. Cross transfusion is an effective means for lowering the non-protein nitrogenous products in the blood of uremic animals.

4. If cross transfusion is started within 90 minutes after intravenous administration of the MLD100 of mercuric chloride, the test animals remain clinically well and their blood creatinine remains normal or nearly normal.

5. If cross transfusion is started within 180 minutes after intravenous injection of the MLD100 of mercuric chloride, the test animals become clinically ill and the blood creatinine rises, but the animals eventually recover.

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